

Remarks

Claims 1-6 and 8-13 were pending in the subject application. By this Amendment, the applicants have amended claims 1, 5, 8, 10, and 11, and canceled claims 6 and 9. No new matter has been added. Support for the amendments to the claims can be found throughout the original specification and claims (see, for example, page 2, line 17; page 3, line 27; page 4, lines 22 and 31-33; page 5, lines 7-8; and original claims 5, 6, and 9). Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 1-5, 8, and 10-13 are before the Examiner for further consideration.

The amendments to the claims have been made in an effort to lend greater clarity to the claimed subject matter and to expedite prosecution. These amendments should not be taken to indicate the applicants' agreement with, or acquiescence to, the rejections of record. Favorable consideration of the claims now presented, in view of the remarks and amendments set forth herein, is earnestly solicited.

Claims 1-6 and 8-13 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Lowe *et al.* (WO 95/26499). The applicants respectfully traverse this ground for rejection because the cited reference does not teach or suggest the claimed invention.

Lowe *et al.* teach detection of an analyte by measuring changes in the properties of a hologram caused by the biochemical interaction between the analyte and the holographic medium (see, e.g., Abstract; page 3, lines 20-25). The biochemical interaction can be between the analyte and a compound immobilized in or on the holographic medium (the receptor; see, e.g., page 3, lines 26-28). For example, an enzyme analyte can digest the holographic medium, or an enzyme analyte can be detected by the substrate (receptor) immobilized in the holographic medium (see, e.g., page 9, specifically lines 9-14). Lowe *et al.* also disclose that detection can be carried out by immobilizing either the analyte or the receptor in the medium (see, e.g., page 13, lines 2-11), and that the analyte can be a cell (see, e.g., page 12, lines 20-25).

In the present invention, on the other hand, cells are not detected by binding to a receptor; instead, the subject invention advantageously identifies the presence and metabolic activity level of cells by detecting a product of their metabolism, germination, or growth. This detection can occur before cell culture properly begins, thus accelerating the analysis process.

In order for this detection process to be possible, there are several technical difficulties that need to be resolved:

- How can the growth medium be provided to the cell in the proximity of the hologram medium?
- Can the cells be immobilized on a planar surface in a way that enables them to be viable and ensure nutrients are available to them from the growth medium?
- Will the product of the metabolic activity be produced by the immobilized cells in an amount sufficient to provide a quick and measurable change in the optical properties of the hologram?
- Will the growth medium properties interfere with the hologram response, for example by masking the response to the product (analyte)?
- Will the pH of the hydrogel of the hologram medium overwhelm the buffer capacity of the growth medium which is necessary to provide appropriate incubation conditions for the cells?
- Will metabolic activity take place when the cell is immobilized in or on the holographic medium?

Lowe *et al.* do not teach or even address how these problems can be overcome. In fact, though the Action suggests that it would be obvious to form a holographic medium out of agar gel or agarose and immobilize the cell or bacterium in this medium, this approach is actually not even possible. Instead, for metabolic activity to be possible, the cell must be immobilized biochemically on a surface in contact with a separate growth medium and close to the hologram medium. In order to achieve a high response of the sensor to metabolic product, it is necessary to operate with small volumes of bacterial cells in a small flow cell volume and flow growth medium over the surface.

The inventors of the claimed invention have advantageously discovered that, in order to retain the cells on the surface under flow conditions, they must be immobilized biochemically, for example, by an antibody. This has the advantages of the flow removing dead cells and other species from the surface, as well as providing specific detection of the cell. Thus, by this Amendment, claim 1 has been amended to emphasize that the cell is immobilized on an antibody. Lowe *et al.*, on the other hand, fail to teach or suggest such a feature. Claim 8 of the subject invention has also been amended to emphasize the distinction over Lowe *et al.* that the chamber also includes an antibody.

Additionally, the applicants respectfully submit that a skilled artisan would have had no reason to modify Lowe *et al.* to arrive at the claimed invention.

As discussed above, Lowe *et al.* teach a method for detection of an analyte by measuring changes in the properties of a hologram caused by a biochemical interaction between the analyte and the holographic medium; the biochemical interaction can be between the analyte and a compound immobilized in or on the holographic medium. Lowe *et al.* do not address any of the many difficulties that would need to be overcome (listed above) and also fail to suggest the possibility of immobilizing a cell on an antibody, as required by the subject invention. In fact, such immobilization on an antibody would not even be possible using the holographic media of Lowe *et al.* Thus, starting with the Lowe *et al.* disclosure, a skilled artisan could not have arrived at the claimed invention without the benefit of hindsight. Hindsight reconstruction of the prior art cannot support a §103 rejection, as was specifically recognized by the CCPA in *In re Spinnoble*, 56CCPA 823, 160 USPQ 237, 243 (1969).

The claimed invention provides a method and device exhibiting good sensitivity in the detection and identification of cells and by-products. The use of an antibody provides, in a single step, specificity, accurate identification, and improvement in flow characteristics. Neither the Lowe *et al.* reference, nor any other prior art document, teaches or appreciates these advantages. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under §103.

In view of the foregoing remarks and the amendments to the claims, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

The applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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Attachment: Request for Continued Examination